REMARKS

Status of the Claims

Claims 1-8 are pending.

Claims 9-11 are hereby canceled.

Reconsideration is respectfully requested. No new matter has been added by the present amendments.

Amendments to the Claims

Claims 1-3, 5 and 6 were amended to remove the teaching of substituent X being "$-CO_2-$."

Claim 4 was amended to replace the phrase "R_4 and R_5 taken together with Z form" with the phrase -- R_4, R_5 and Z are represented by --.

Rejections Under 35 U.S.C. §112, 1st ¶

Claims 8-11 were rejected under the first paragraph of 35 U.S. C. § 112 because the specification allegedly does not reasonably provide enablement for treating any or all inflammatory disorders specifically embraced in the instant invention. The Examiner further asserts that the specific diseases taught in the instant claims are allegedly not enabled by the present disclosure.

Applicants have canceled claims 9-11 from the instant case.

Applicants will hereby provide support in the form of publications (attached herewith) to show that one skilled in the art would recognize that the instant specification would reasonably provide enablement for the disorders taught in Claim 8. Firstly, as disclosed in the instant specification, it is known by one skilled in the art that the p38 mitogen-activated protein kinase (MAPK) signalling pathway plays an important role in inflammation and other physiological processes. J. Saklatvala, "The p38 MAP kinase pathway as a therapeutic target in inflammatory disease," Current Opinion in Pharmacology, 2004, 4:372-377, 372; and J. Branger, et al., "Anti-Inflammatory Effects of a p38 Mitogen-Activated Protein Kinase Inhibitor During Human Endotoxemia," The Journal of Immunology, 168, 4070-4077 (2002). It is further known that

P38-α signaling and TNF-α regulation has been shown to be involved in the pathogenesis of inflammatory bowel disease -- Crohn's disease and ulcerative colitis. G.H. Waetzig, et. al., "p38 Mitogen-Activated Protein Kinase is Activagted and Linked to TNF-α Signaling in Inflammatory Bowel Disease," The Journal of Immunology, 168, 5342-5351 (2006).

Lastly, studies have identified p38 MAPK as a novel therapeutic target to overcome drug resistance and patient outcome in multiple myeloma. T. Hideshima, et al., "Targeting p38 MAPK Inhibits Multiple Myeloma Cell Growth in Bone Marrow Milieu," Blood, 101, 703-705 (2003); and T.A. Navas, et. al., "Inhibition of p38-α MAPK enhances Proteasome Inhibitor-induced Apoptosis of Myeloma Cells by Modulating Hsp27, Bcl-X_L, Mcl-1 and p53 Levels *in vitro* and Inhibits Tumor Growth *in vivo*," Leukemia, 1-11 (2006).

Consequently, one skilled in the art would recognize that the compounds taught by the present invention would inhibit p38-α and affect TNF-α regulation in a similar manner as described in the above-cited references, such that the instant specification is enabling for treating the indications identified in Claim 8. As a result, applicants believe that the rejection under the first paragraph of 35 U.S.C. § 112 has been overcome and should be kindly removed.

Rejections Under 35 U.S.C. §112, 2nd ¶

Claim 4 was rejected under the second paragraph of 35 U.S. C. §112 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserts that there is insufficient antecedent basis for the limitation "R_4 and R_5 taken together with Z form" the "NH-phenyl moiety" in line 3 of said claim. Applicants have amended line 2 of claim 4 to replace the phrase "R_4 and R_5 taken together with Z form" with the phrase -- R_4, R_5 and Z are represented by --. Antecedent basis for this amendment can be found in claims 1 and 3. Thus, the instant amendment should obviate this rejection under the second paragraph of 35 U.S.C. §112, which should now be kindly removed.

Rejections Under 35 U.S.C. §103(a)

Claims 1-11 were rejected under 35 U.S. C. §103(a) as allegedly being unpatentable over Hunt, et al. (U.S. Pat. No. 6,982,265).

Specifically, claims 1-11 were rejected in view of Example 19 in Hunt, et al. Applicants have amended claims 1-3, 5 and 6 to remove the teaching of substituent X being "$-CO_2-$", so this rejection of claims 1-11 should be obviated and kindly removed.

Claims 5 and 6 were also rejected as being allegedly obvious in view of Hunt, et al. Applicants do not fully comprehend this rejection because it is not clear which part of Hunt, et al. discloses "the method of using compounds where X-R_2 = N-R_{10}CO-alkyl; Y = absent; R_3 = substituted alkyl; R_5,R_1 = H; R_6 = H, alkyl; Z = N; R_4 = sulfonamide substituted aryl." Then, the Examiner asserts, "[t]his compound is the instant compound where X-R_2 = N-R_{10}CO-alkyl (R_{2a},R_{10} = H); R_3 = Me or trifluoro methyl; R_1,R_5 = H; R_6 = H, alkyl; Y = SO_2NH (sulfonamide)." This second assertion is also confusing because while instant claim 5 teaches that substituent X can be "–N-R_{10}C(=O)–", this does not comport with the teaching of substituents R_{2a} and R_{10} in claim 6, which cover the teaching of X as "–C(=O)NR_{10}–." Thus, applicants kindly request clarification of rejections claims 5 and 6.

Fees

If it is determined that a fee is due, please charge same to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

SUMMARY

In view of the foregoing comments and amendments, applicants kindly request reconsideration of the application. Applicants believe the case is now in condition for allowance and respectfully request the Examiner to pass the case to issue at an early date.

Respectfully submitted,

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